ISOQUINOLINE DERIVATIVES HAVING KINASE INHIBITORY ACTIVITY AND MEDICAMENT CONTAINING THE SAME

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BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to i /atives having Rho kinase inhibitory activity, more particu ne derivatives useful for the treatment of diseases media e.

Background Art

It has been revealed that Rho is activated upon the receipt of signals from various cell membrane receptors, and the activated Rho functions, through ROCK/Rho kinase and, further, actomyosin system, as a molecular switch of a wide variety of cellular phenomena such as smooth muscle contraction, cell movement, cell adhesion, change in character of cells (formation of actin stressed fibers), control of cell division (sthenia of cytokinesis or activation of gene transcription), platelet aggregation, leukocyte aggregation, cell proliferation, sthenia of carcinogenesis and invasion of cancer and the like.

The contraction of smooth muscle is deeply involved in the pathology of hypertension, angina pectoris, vasospasm, for example, cardiovascular contraction and cerebrovascular contraction, asthma, peripheral circulatory disorder, threatened premature birth, glaucoma, constriction of visual field, pollakiuria, impotence and the like. Cell movement plays an important role in invasion/metastasis of cancer, arteriosclerosis, retinopathy, immune response and the like. Cell adhesion is deeply involved in metastasis of cancer, inflammation, and autoimmune diseases. The change of cell morphology is deeply involved in cerebral dysfunction, osteoporosis, microbism and the like. Cell proliferation is deeply involved in cancer, arteriosclerosis and the like. Thus, Rho is deeply involved in various diseases.

ROCK or ROCK I (Japanese Patent Laid-Open No. 135683/1997; and T. Ishizaki et al., EMBO J., Vol. 15, No. 8, pp 1885-1893 (1996)) and Rho kinase or ROCK II (Japanese Patent Laid-Open No. 113187/1998; and T. Matsui et al., EMBO J., Vol. 15, No. 9, pp 2208-2216 (1996)) were reported as serine/threonine kinase which is activated upon the activation of Rho and were shown to be isozymes (O. Nakagawa et al.,